22. Toxins, health, and behavior: implications of toxicology for public policy

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1. INTRODUCTION: EFFECTS OF LEAD AND MANGANESE ON HUMANS

Within universities, studies of the impact of toxins on behavior or health are endangered by the divisions between departments in the Natural and Social Sciences. Toxicologists focus on the danger of chemicals, often in laboratory testing; political scientists study factors shaping the way public issues are perceived and the effects of political decisions. In the new field of Biology and Politics, these issues are addressed by linking harmful effects of toxins to behaviors such as educational failure, substance abuse, and violent crime (Gottschalk et al., 1991) with results useful to both decision-makers and the general public (Masters et al., 1998).

To start with lead, widely known to be harmful, toxicologists who study its harmful effects typically measure the danger by calculating "LD50" – that is, the exposure that has a 50 percent probability of lethal effects. Such harmful effects have been known in America since Benjamin Franklin, who wrote on the "danger of lead taken inwardly" (1786 [1987]). In recent years, many toxicological studies have focused on exposures far below the "LD50" level that have negative effects on widespread behaviors with enormous costs to taxpayers (Struempler et al., 1985).

For example, the traditional measure of dangerous environmental exposures to lead has been 10 micrograms per deciliter (µg/dL) of drinking water. Although this may seem a small amount, in reality there are often cumulative effects from lead in municipal water supplies, lead pipes joined with lead solder, residues of lead paint in old housing, industrial lead pollution, and other lead elements in the environment. (Bratton et al., 1994; Wright et al., 2008). Several years ago, a "Toxic Substances Control Committee" formed by the Vermont state government recommended that since it was impossible to find a "safe" level of exposure to lead, the level justifying intervention by the state Department of Health or other public authorities in Vermont should be reduced to 5µg/dL. This decision was a compromise to reflect new scientific studies without blatantly offending powerful interests.

Manganese is another element that has toxic effects on humans (Kirpekar et al. 1970; Autissier et al., 1982; Massie, 2010). Since both lead and manganese are found in many water systems, problems often occur when either one or both are present in the tap water of Americans. Recent research has also revealed harm from the substitution of either fluorosilicic acid (H_2SiF_6) or sodium silicofluoride (Na_2SiF_6) for sodium fluoride (NaF) as the compound used for "water fluoridation" in communities which now serve over 120 million Americans (Masters and Coplan, 1999a). These three toxins (either alone or in combination) have been associated with increased blood lead levels in a local community, with effects on learning behavior, substance abuse, and violent crime.

Mechanisms for these effects have been discovered by toxicologists or other biological specialists in human brain chemistry. Both lead and manganese reduce the activity of neurotransmitters that often play an inhibitory role in behavior and learning. Lead lowers the action of dopamine (Struzynska and Rafalowska, 1994; Zuch et al., 1998); and norepinephrine (Bratton et al.,1994). Manganese also reduces the functional activity of norepinephrine (Kirpekar et al., 1970; Massie, 2010) and dopamine (Autissier et al., 1982). Moreover, where water is treated with a silicofluoride – that is, either fluorosilicic acid (H2SiF6) or sodium silicofluoride (Na2SiF6) – research shows that the lead in children's blood is significantly increased (Masters and Coplan, 1999b; Masters et al., 2000). In addition, silicofluorides inhibit the activity of the enzyme acetylcholinesterase, which regulates the neurotransmitter acetylcholine, a major neurotransmitter activating human muscles and hence human activity (Finney et al., 2006). These effects of lead, manganese, and silicofluoride are linked to hyperactive behaviors associated with behavioral (and especially learning) problems that are more frequent where lead and manganese are polluting the environment (Coplan and Masters, 2001).

The present study describes tests of the association between localities in which the population is exposed to lead, manganese, or silicofluoride and public statistics showing harmful effects on human health or behavior. The analysis has three major components. First, an assessment of the harmful effects of toxins, illustrated by lead and manganese, can illustrate why the assessment of superfund sites needs to consider multiple toxins as well as a range of their behavioral and health effects. Second, the harm from chemical compounds (silicofluorides) now used for over 90 percent of water fluoridation in the United States illustrates how failure to conduct such analysis is today poisoning well over 120 million Americans. Third, generalization of these two examples not only identify toxic chemicals that increase learning disabilities, substance abuse, and violent crime, but reveal sources of disproportionate harm to some minorities that conventional social scientists have never suspected.

2. EXAMPLE: SILICOFLUORIDES IN PUBLIC WATER

Over the last fifty years, extensive controversy has raged over the "fluoridation" of public water supplies (Bryson, 2004; Rymer, 2000; Shabecoff and Shabecoff, 2008). Energetically promoted by the American Dental Association and Centers for Disease Control (CDC) as a means of reducing tooth decay and improving dental health, others claim the practice of adding fluoride to public water produces unsightly stains on teeth (dental fluorosis) and has little beneficial effect. For example, while Bryson cites data showing that the beneficial effects of fluoride on tooth decay occur from topical applications on the tooth surface, he also cites research showing that the effects of fluoridation sometimes produce mottled teeth or other harmful effects. Of policy importance, however, are reports of tooth decay showing that rates of caries – among minorities – are *worse* in communities that "fluoridate" their water supply (one example is Harlem). Probable reasons for these findings may be associated with a major flaw in the debates of the last half-century.

For practical reasons it is impossible to add "pure" fluoride to a water supply. The public policy called "fluoridation," whether by supporters or by critics, relies on one of three chemical compounds. These chemicals are sodium fluoride (NaF) and one of two compounds called "silicofluorides:" hydrofluorosilicic acid (H2SiF6) and sodium silicofluoride (Na2SiF6). The compound chosen by a public water system greatly influences users' processing of the treated water and its effects on health and behavior. The principal difference, well documented in many comparative studies but ignored when an EPA administrator provided advice to a Congressional committee in 1999, is that silicofluorides consistently produce *different* biological effects than sodium fluoride (Fox, 1999; Coplan and Masters, 1999).

Both supporters and critics continue to call this public policy "fluoridation," without reference to the different compounds used for the purpose. This scientifically vague practice began in public statements by proponents in the 1940s, and unfortunately has been followed regardless of policy preferences (Waldbott et al., 1978; Cohn, 1992; Reeves, 1994). For purposes of public policy decision-making and assessment of outcomes, reference to each of the chemicals used is highly advisable.

Sodium fluoride is the only compound for which careful scientific testing was conducted either before or after its usage for water fluoridation began. The use of sodium fluoride has been justified because harm is prevented by the chemical "dissociation" between the sodium (Na) and fluoride (F) atoms when sodium fluoride (NaF) is added to water. The possibility of harmful side-effects from silicofluoride-treated water follows from the presence of silica, an atom with eight bonding sites (that is, it forms a bond with eight other atoms). This means that while a silicofluoride carries six fluoride atoms, it also carries both one silica atom and two other atoms (either hydrogen or sodium), making possible biochemical results that do not occur when water is treated with sodium fluoride.

Although the American Dental Association and other supporters, including the American Public Health Association and Centers for Disease Control (CDC), have followed the unscientific practice of speaking *only* of "fluoridation," ignoring the different compounds used for this purpose, public policy-makers should not continue to make this mistake. Where silicofluorides are in use, uptake of lead from environmental sources like old housing with lead paint is higher than where water is treated with sodium fluoride or not fluoridated. Our data for epidemiological studies of children's blood lead levels (Tables 22.1 and 22.2; Figures 22.1 and 22.2) has included three samples with a total population of over 400 000 (children in Massachusetts and New York and in the National Health and Nutrition Examination Survey (NHANES III). These effects are significantly worse for poor and especially poor black children (probably due to lower levels of calcium in their diet, in turn probably due to lactose intolerance).

Many behavioral dysfunctions have been associated with lead neurotoxicity by well-known researchers (for example, Needleman, 1989). Controlling for other risk factors, we have found a number of these dysfunctions are significantly higher in communities that treat water with silicofluorides than in those using either water treated with sodium fluoride, naturally fluoridated water, or untreated water (Coplan and Masters, 1999; Wilson, 1999; Seavey, 2005; Maas et al., 2007; Masters, 2001). Among these behaviors are rates of violent crime (assessed using national data by county for two different years), substance abuse (using data from a National Institute of Justice study of cocaine use at time of arrest

Table 22.1 Percent screened with blood lead above 10µg/dl and other characteristics: matched sample of 30 nonfluoridated and 30 silicofluoride communities, Massachusetts

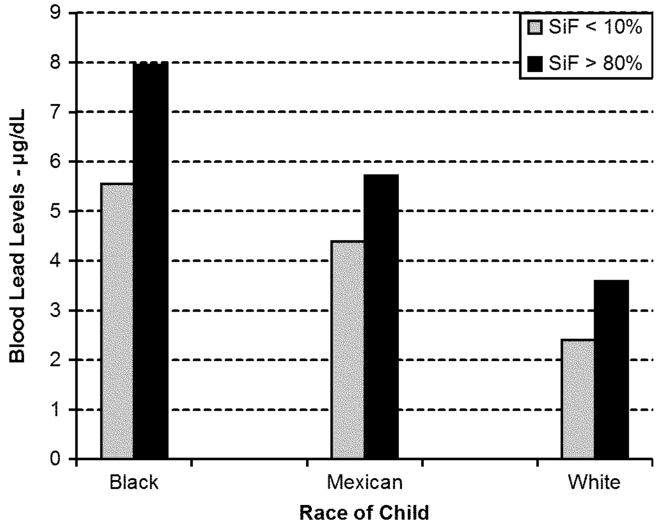
	30 Non-fluoridated Communities	30 Fluoridated Communities
Population(1000s)	837.3	845.1
Children 0–5	57 031	56 446
% children screened w/ >10 µmg/dL	**0.76**	**1.94**
Lead in water (ppb)	21	30
4th grade MEAP	5440	5455
% Poor	4.6%	5.1%
% Nonwhite	6.6%	11.5%
% AB.	23.6%	30.5%
Income per capita	$116 600	$19 600

Source: Masters and Coplan (1999b).

Table 22.2 Community demographics and risk factors, NY sample: distribution of 1990 US census variables in 105 NY state communities of population 15 000–75 000 by SiF status

	SiF	No SiF
Demographics of 105 communities		
Number of Communities	28	77
Mean Community Size	34 778	25 627
Children 0–5 as % of Pop.	8.50%	8.00%
No. Children 0–5 per Community	2960	2046
Total number children tested 1994–98		
Total Number of VBL Tests	56 934	94 291
Total Number Capillary Tests	36 791	68 357
Total of all Blood Lead Tests	93 725	162 648
Percent of Tests for VBL	61%	58%
Seven risk-factors associated with high blood lead		
Housing pre-1939	49.4%	23.3%
% Age 0–5 in Poverty	22.3%	8.5%
% Unemployed	3.5%	2.5%
% B.A.	7.4%	9.3%
Pop density (per Sq. Km)	155	143
Total Population	973 785	1 973 336
Per Capita Income	$14 698	$19 415

Source: Masters et al. (2000).



Notes: For NHANES III Children 3–5, mean blood lead is significantly associated with fluoridation status (DF 3, F 17.14, p < .0001) and race (DF 2, F 19.35, p < .0001) as well as for poverty income ratio (DF 1, F 66.55, p < .0001). Interaction effect between race and fluoridation status: DF 6, F 3.333, p < .0029.

Figure 22.1 Average blood lead: NHANES III, children aged 3–5: counties over 500000

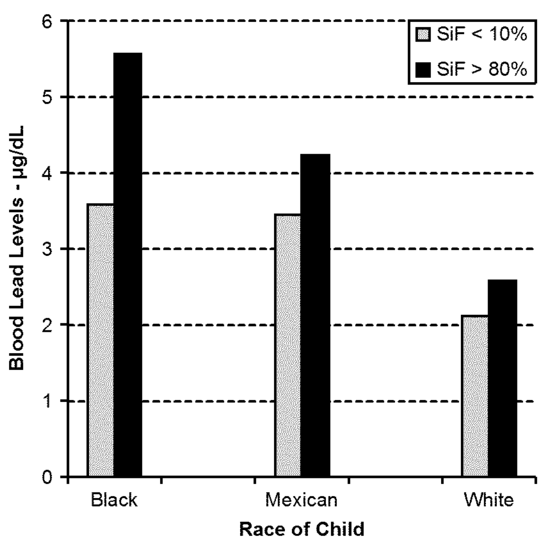


Figure 22.2 Average blood lead: NHANES III, children aged 5–17: counties over 500 000

Table 22.3 US average rates in cities for six crimes by fluoridation chemical

	MURDER		RAPE		ARSON
	2000	2001	2000	2001	
Silocofloride					
H2SIF6	48.51	52.38	157.46	163.01	173.29
Na2SiF6	43.02	112.88	182.22	184.95	160.82
NaF	27.86	27.14	134.86	131.57	117.43
Natural	12.86	11.86	90.0	76.0	69.86
None	18.3	16.54	106.5	100.0	128.77
# of cities	145	148	139	141	137

Note: In addition to variation in number of cities reporting for each type of crime,the size of city is a major variable (see Table 22.2). As a result, these statistics are provisional, requiring further multivariate analysis to confirm that effects of silicofluorides in public water supplies that were found in US county data for violent crimes in two earlier years are also present in this recent data by city.

Source: Crime rates: FBI (2002). Fluoridation agent: CDC Fluoridation census (1992).

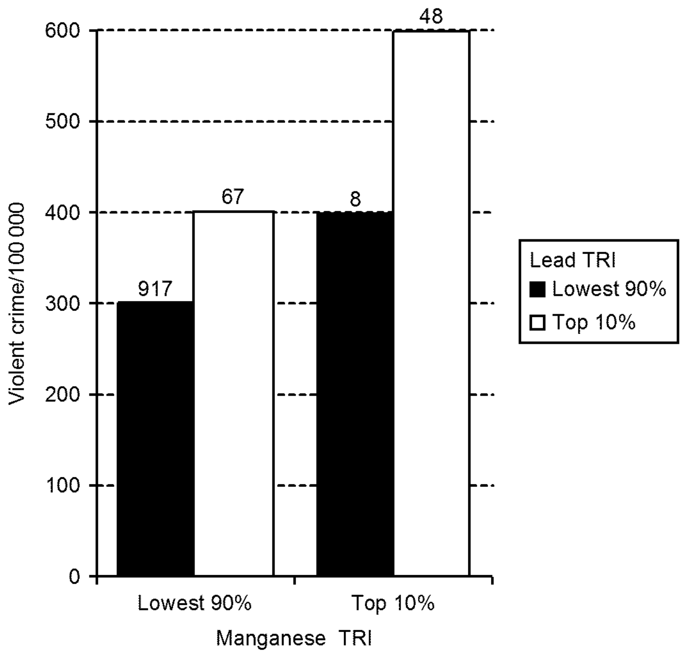
for crime), and learning disabilities (ADHD having widely been found to have, among possible causes, lead uptake).

The association between lead uptake and violent crime rates is confirmed by recently released FBI crime data by city for the years 2000 and 2001 (Table22.3). While less comparable data are availablefor enhancement of the behavioraleffects of manganese toxicity, limited data using the EPA'stoxic release inventory indicates that there is probably a similar interaction for this toxin as well (Table22.2). In all of these cases, however, crude measures of association need to be assessed using multivariate statistical techniques to control for other risk variables. Using different data analyses and controlling for other risk factors in a variety of databases,silicofluoride treatment of water supplies has repeatedly been found to be an additional factor contributing to costly behavioral dysfunctions (Tables 22.4–22.9).

In the light of these findings, an immediate moratorium on use of silicofluorides in public water supplies is needed until extensive testing has conclusively demonstrated their safety.Such testing must include not only the chemical effects of adding silicofluorides to water (which are the first item listed by the National Toxicology Program (NTP) in their official "nomination" of silicofluorides for toxicological study), but also experimental studies of the costly behavioral effects found in analyses cited above.

Public policy action on this research is more than justified since over 120 million Americans are now exposed to these untested toxic chemicals in their water supplies. From the studies cited here, epidemiological data show negative outcomes are worse for some ethnic minorities than for Whites. Increased rates of violent crime associated with silicofluorides have resulted in the highest rate of per capita incarceration among the industrial nations of the world. Since a year in jail costs $30000 or more (depending on the jurisdiction), not to mention the costs of higher rates of learning disabilities and substance abuse, silicofluoride-treated water entails substantial costs to taxpayers.

Finally, claims by dental associations that rates of tooth decay have been reduced by



Note: Dataset of 2899 US counties reporting both TRI (EPA Toxic Release Inventory) and violent crime (FBI Uniform Crime Statistics).

Source: Masters et al. (1998).

Figure 22.3 Environmental pollution with lead and manganese and rates of violent crime: US counties

"fluoridation" have been contested because rates of caries are similar in Europe (where silicofluorides are not added to water) and the US. But even if water treatment with silicofluorides actually did reduce dental costs, the harmful effects to health and behavior are documented by scientific studies linking brain chemistry to behavior (a field outside the scientific competence of the American Dental Association). It is worth adding that the foregoing comments do not concern the use of sodium fluoride, which still can be used for dental health.

3. THE NEW PERSPECTIVE REQUIRED FOR RESEARCH ON HEAVY METALS, HEALTH, AND BEHAVIOR

The above analysis is based on extensive work in recent years on health and behavior following the effects of heavy metals (primarily lead and manganese) as well as the research on "silicofluorides" (Bryson, 2004). This research and the professional collaboration it has entailed indicate three principles for policy-making on issues concerning toxins, pollution, and health or behavior.

Table 22.4 Multiple regression analysis of violent crime rates in US, 1991

Variable	Unstandardized Coeff.	T-ratio	Probability
Population Density	82.42	20.24	<.0001
Per capita income	−.0007	−2.74	<.0001
Unemployment	NOT SIGNIFICANT		
%Black Poverty	40.06	2.33	<.05
% Hispanic Poverty	62.11	2.79	<.005
Police per Capita	153423	l6.56	<.0001
Infant Death Rate	1.813	2.78	<.005
% housing pre 1950	526.75	−13.43	<.0001
Public water/cap	225.34	4.07	<.0001
Median Grade Complete	24.68	3.50	<.005
LeadTRI present	40.80	4.67	<.0001
ManganeseTRI	58.71	6.68	<.0001
Alcohol Death Rate	101.62	11.55	<.0001
#Alcohol & Lead	21.48	2.54	<.05
#Alcohol & Manganese	55.40	6.54	<.0001
#Lead & Manganese	34.89	4.11	<.0001
#Alcohol & Lead& Manganese	19.21	2.27	<.05

Notes: Adjusted r-square: 0.369. F 97.45; DF 17.2783; p − .0000
– interaction terms.

Source: Masters et al. (1998).

Principle 1: New ways of thinking are needed to understand environmental factors (including toxins like mercury) that influence health and behavior.

- *Because individuals and groups differ in vulnerability, it is necessary to use an interactive approach that goes beyond the traditional search for a single "cause" of all problematic behaviors.* Examples include: first, a recent study showing how the interaction of a mutant MAO A gene (on the X chromosome) and experience of childhood abuse lead to antisocial personality (Caspi et al., 2002); second, the association between lactose intolerance (a genetic trait common among Blacks and some other ethnic groups) and enhanced uptake of lead from the environment (see Figures 22.1 and 22.2; Angier, 1993; Reif et al., 1993). And finally, as illustrated by the time lag between exposure to leaded gasoline and lead uptake, infants are often especially at risk for uptake during fetal development and the first months of life (NIMH) with a time lag until effects are documented.
- *Since the same effect or phenotypic trait can have multiple causes, it is necessary to go beyond the traditional medical practice of linking "one germ to one disease."* For example, hyperactivity (ADHD) has been traced to genetic mutation, to uptake of toxins and their effects on dopamine and neurotransmitter function, and to social experiences such as abnormal events in early childhood (Masters, 2001). Similarly, Alzheimer's disease has been traced to uptake of aluminum, to alcohol consumption, and to social isolation.

Table 22.5 Factors influencing US violent crime rate, 1985: multiple regression, 2880 US counties

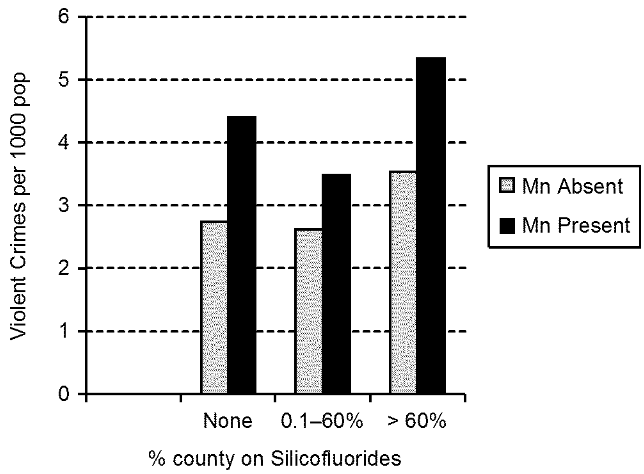
Variable	Standardized Coefficient	t-value	Probability
% Black	.2798	15.895	.0001
Poverty/Wealth Ratio	.2262	6.564	.0001
Population Density	.1956	9.383	.0001
% SiF	.1150	6.191	.0001
% HS Graduate	.0795	3.461	.0005
Per Capita Income	.0457	1.851	.0642
% Houses pre 1939	−.1071	5.091	.0001
Population	−.02587	0.823	n.s.
Lead Toxic Releases	.0042	0.262	n.s.
Manganese Toxic Releases	.0196	1.246	n.s.

Notes:
DF 10, 2869; R squared = .3238; F-test = 137.401; p = .0001.
Variables listed in order of strength of standardized coefficient.
When both % of population on silicofluorides and toxic release inventory (TRI) of lead and manganese are included in the analysis, silicofluoride usage is a significant predictor of violent crime whereas heavy metal pollution ceases to have a significant additional effect. This probably explains the significance of the variable "public water supply per capita" in the 1991 multiple regression in Table 22.4, which was calculated before RDM knew of the issue of silicofluoride toxicity.

Principle 2: Because nothing acts alone, it is essential to study interactions between various factors that influence health and behavior.

- *Multiple toxins have worse effects than each of these toxins alone.* For example, uptake of lead and of manganese has worse effects on behavior than either toxin alone (Figure 22.3; Table 22.4). Uptake of a toxin that inactivates metallothionein (for example, by changing this protein's three-dimensional conformation) results in failure of this natural mechanism for sequestering and excreting toxins. As a result of such processes, the addition of fluoride compounds has also been found to be problematic. For example, in 1997, a Federal government report found that "for small systems using ground water . . . the second leading problem . . . was fluoride, which was reported as a problem by 57 (8.8 percent) of the small ground water systems with violations" (National Research Council, 1997, p32). Although silicofluorides (H2SiF6 or Na2SiF6) are used for over 90 percent of water fluoridation in the US (and currently treats water delivered to over 120 million Americans), this report did not distinguish between compounds used to add fluoride.
- This failure to distinguish between sodium fluoride and silicofluorides is also relevant to the NRC report that:

> Copper and fluoride were the most frequently identified chemicals causing acute illness – usually vomiting within a short time after consuming the water or using it in beverages. The source of copper in these outbreaks was leaching from plumbing and water service pipes due to corrosive water.. . The source of fluoride was various operational and technological deficiencies in the equipment used to fluoridate the water to prevent dental



Notes:
Significance: Silicofluoride Usage: p = .0001, F 27.605; Manganese Pollution: p = .0001, F 79.005; Interaction of SiF and Mn: p = ..0239, F 3.739.
For the 369 US counties where over 60% received water treated with silicofluorides, and there is no Toxic Release Inventory record for manganese, the violent crime rate in 1991 (3.53 per 1000) was intermediate between rates in the 109 counties with manganese TRI and no silicofluorides (4.40) or the 217 counties with between 0.1 and 60% receiving silicofluorides (3.49). Where both silicofluorides are delivered to over 60% of the population and manganese TRI is present, the crime rate was 5.34. In 1991, the national county average was 3.12 violent crimes per 1000.

Figure 22.4 Manganese TRI and silicofluorides as factors in violent crime, 1991

problems. Two deaths occurred as a result of high fluoride levels (National Research Council, 1997, p.38).

- Because silicofluorides are highly corrosive compounds, it is likely that some of the effects of copper water pipes were influenced by the use of silicofluorides (Hara et al., 2002; Coplan and Masters, 1999). Such an effect, especially when combined with water disinfected by either chlorine or chloramine, would be parallel to the experimental finding that when silicofluoride is combined with chloramine or chlorine, substantial amounts of lead leach from brass pipes or water meters (Maas et al., 2007). As these findings confirm, speaking of "fluoride" without reference to the specific compounds used in fluoridation and ignoring interactions between chemicals can result in failure to consider effects like those produced by the interaction between silicofluoride and chloramine as a source of lead leached from either leaded solder or brass water fixtures.
- *Biomarkers that measure the exposure and uptake of chemicals have an essential role to play in monitoring and analyzing risks to health and behavior.* While it was long traditional to measure levels of lead and other toxins in blood, sampling urine or head hair is also valuable and in some cases more effective as a screening device. For a precise measure of uptake of a single toxin, it may be necessary to analyze more than one biomarker (for example, verifying lead levels in head hair by

Table 22.6 Multiple regression: causal factors associated with rates of violent crime, all US counties, 1985

Variable:	Coefficient	Std. Err.	Std. Coeff.	t-Value	Probability:
Intercept	−0.005056				
**%SiF	0.000368	0.000133	0.044933	2.779132	0.0055
Unemployment	0.000076	0.000013	0.106014	5.988623	0.0001
Per capita Income Black	−9.92E-09	5.69E-09	−0.028883	1.742151	0.0816
Per capita Income	9.53E-08	1.91E-08	0.115025	4.989345	0.0001
Median Grade Completed	0.000205	0.000069	0.081833	2.971707	0.003
Median Year Housing Built	0.000003	0.000004	0.01226	0.719065	0.4722
% Black	0.00005	0.000003	0.313211	17.565442	0.0001
% Graduate	−0.000022	0.000007	−0.096468	2.965084	0.0031
% Rural	−0.000027	0.000001	−0.349944	18.728391	0.0001

Confidence Intervals

Variable:	95% Lower:	95% Upper:	90% Lower:	90% Upper:	Partial F:
Intercept					
**%SiF	0.000108	0.000628	0.00015	0.000587	7.723575
Unemployment	0.000051	0.000101	0.000055	0.000097	35.863607
Per capita Income Black	−2.11E-08	1.25E-09	−1.93E-08	−5.50E-10	3.035091
Per capita Income	5.78E-08	1.33E-07	6.39E-08	1.27E-07	24.893561
Median Grade Completed	0.00007	0.00034	0.000091	0.000318	8.831041
Median Year Housing Built	−0.000005	0.000011	−0.000004	0.00001	0.517055
% Black	0.000044	0.000056	0.000045	0.000055	308.544769
% Graduate	−0.000036	−0.000007	−0.000034	−0.00001	8.791723
% Rural	−0.00003	−0.000024	−0.000029	−0.000024	350.752619

Note: Again, presence or absence of silicofluorides is a significant predictor of violent crime. Interestingly, in this group of nine predictive variables, only the median year of house construction is *not* significant.

analyzing lead levels in blood). On the other hand, for environmental assessment and epidemiological research, head hair has the advantage of measuring cellular uptake of 17 toxins and 23 necessary elements simultaneously by using a non-invasive sample of head hair that is easily obtained and relatively inexpensive (Quig, 1997).

Principle 3 Policy interventions can be important: "an ounce of prevention is worth a pound of cure."

In this process, science matters, as is illustrated by the evidence that the ban on leaded gasoline had the effect of reducing rates of violent crime (see Table 22.4) while the practice of water fluoridation with silicofluorides significantly increased rates of violent crime (Coplan and Masters, 1999; Wilson, 1999; Seavey, 2005; Masters et al., 1999). Because most citizens (and indeed most social scientists) are not fully aware of the scientific complexities just described, principles of market allocation don't always work to prevent harm from toxins (as illustrated by the continued use of dental amalgam after dangers

Table 22.7 Multiple regression: causal factors associated with rates of violent crime, all US counties, 1991

Variable:	Coefficient	Std. Err.	Std. Coeff.	t-Value	Probability
Intercept	−0.026874				
**%SiF	0.000922	0.00019	0.076136	4.847215	0.0001
Unemployment	0.000064	0.000017	0.062928	3.693542	0.0002
Per capita Income Black	−3.96E-09	8.09E-09	−0.007926	0.489639	0.6244
Per capita Income	1.28E-07	2.63E-08	0.108872	4.869223	0.0001
Median Grade Completed	0.000504	0.000095	0.140963	5.304905	0.0001
Median Year Housing Built	0.000014	0.000006	0.039495	2.411564	0.0159
% Graduate	−0.000058	0.00001	−0.178521	5.719072	0.0001
% Rural	−0.000041	0.000002	−0.376415	20.749842	0.0001
% Black	0.00008	0.000004	0.351002	20.358866	0.0001

Confidence Intervals

Variable:	95% Lower	95% Upper	90% Lower	90% Upper	Partial F
Intercept					
**%SiF	0.000549	0.001295	0.000609	0.001235	23.495494
Unemployment	0.00003	0.000098	0.000035	0.000092	13.642253
Per capita Income Black	−1.98E-08	1.19E-08	−1.73E-08	9.36E-09	0.239747
Per Capita Income	7.65E-08	1.80E-07	8.48E-08	1.71E-07	23.70933
Median Grade Completed	0.000317	0.00069	0.000347	0.00066	28.142022
Median Year Housing Built	0.000003	0.000026	0.000004	0.000024	5.81564
% Graduate	−0.000078	−0.000038	−0.000075	−0.000041	32.70778
% Rural	−0.000045	−0.000037	−0.000044	−0.000038	430.555948
% Black	0.000072	0.000088	0.000074	0.000087	414.483444

Note: In 1991, silicofluorides are again a signicant predictor of violent crime controlling for eight other variables. Unlike 1986, in 1991 age of housing is a significant predictor whereas per capita income among blacks is no longer significantly associated with rates of violent crime in the US.

from mercury were identified by specialists). Overall, especially given the characteristics of public health and environmental protection as "public goods," government has a necessary role to play. Regulations and laws can play a valuable role in protecting the public, including not only prohibitions of commercial sale of known toxins, but also the enforcing principle that untested chemicals shouldn't be added to a public water supply until they are shown to be safe. Judicial procedures can also play an essential role by establishing and enforcing liability for damages due to the use of known toxins in a manner fair to both those seeking and those opposed to exposing the public to the chemical in question.

Table 22.8 Effect of fluoridation chemicals on crime rates in US cities by size (2000, 2001)

	Silicofluoride	Other	Totals
Murder 2000			
<250000	16.06 (66)	14.25 (24)	15.58 (90)
250–750000	44.87 (38)	33.2 (5)	43.51 (43)
>750000	258.8 (10)	42 (2)	222.67 (12)
Total	**46.96 (114)**	**19.10 (31)**	**41.0 (145)**

Signif:
size of city = .0001; fluoridation chemical = .0002; interaction =.0003

Murder 2001			
<250000	16.58 (67)	13.0 (25)	15.61 (92)
250–750000	50.10 (39)	31.6 (5)	48.0 (44)
>750000	554.2 (10)	43.0 (2)	469 (12)
Total	**74.20 (116)**	**17.78 (32)**	**62.0 (148)**

Signif:
size of city = .0323; fluoridation chemical = .0334; interaction =.0623

Rape 2000			
<250000	79.48 (62)	87.35 (23)	81.61 (85)
250–750000	213.45 (38)	196.6 (5)	211.49 (43)
>750000	584.56 (9)	180.5 (2)	511.09 (11)
Total	**167.89 (109)**	**111.77 (30)**	**155.78 (139)**

Signif:
size of city = .0323; fluoridation chemical = .0334; interaction =.0623

Rape 2001			
<250000	81.43 (63)	81.83 (23)	81.53 (86)
250–750000	222.03 (39)	172.4 (5)	216.39 (44)
>750000	592.56 (9)	159.0 (2)	513.73 (11)
Total	**172.27 (111)**	**102.07 (30)**	**157.33 (141)**

Signif:
size of city = .0001; fluoridation chemical = .0048; interaction =.0431

4. SUPERFUND SITES, HEALTH AND BEHAVIOR: STUDIES OF TOXIGENOMIC EFFECTS OF ABANDONED MINES

A second example of the new approaches to policies on the environment, health and behavior is provided by research on two abandoned mining sites in Quebec. Under the direction of Christopher Covel, a geologist now of Jefferson, Maine, preliminary research has identified the toxins in mine tailings and water polluted by an abandoned mine at Lake

Chibougamau, Quebec, comparing chemicals present in the environment with uptake of these toxins by members of the Oujé-Bougoumou Cree community living at this site. This field research thus explored how the association between exposure and uptake could illuminate levels of disease and behavioral dysfunction among the Cree. A similar study has been conducted on effects of exposure to toxins from another abandoned mine on the Kanesatake Mohawk community near Oka, Quebec.

A brief review of this research on abandoned mines will illustrate the need to reconsider the analysis of exposure to multiple toxins at Superfund Sites throughout the US. Because evidence of effects on health and behavior is focused on members of two Native American communities, these cases allow study of multiple toxins and their effects with minimal confusion of genetic diversity and population mobility. The Oujé-Bougoumou Cree, living near Chibougamau, Quebec (about 300 miles north of Montreal), are exposed to residues from abandoned copper and gold mines (Covel, 2001). The Kanesatake Mohawk, living near Oka, Quebec, are affected by contaminated soil and water due to what was the world's largest mine for niobium (a rare metal used to harden steel). In both communities, extremely high levels of toxins were found in soil and water. Analysis of head hair from small exploratory samples in each community revealed cellular absorption of dangerous levels of multiple toxins in many children and adults. Moreover, if head hair has absorbed a toxin, it is prudent to assume this has also occurred in the brain's neurons.

To summarize briefly data on toxins in head hair among the Oujé-Bougoumou Cree, it is useful to consider the 95 percent percentile level of each toxin for adult males and females as a measure of unquestioned harm. To illustrate, for four well-known toxins, the following proportions of those we sampled were over the 95 percent percentile (that is, less than 5 percent of those sampled were as high or higher): mercury – 12 of 22 reports; manganese – 7 of 22 reports; arsenic – 3 of 22 reports; antimony – 7 of 22 reports. To interpret these results, it needs to be noted that 1.1 cases out of 25 tested represents the average number of Americans above the 95th percentile. For these four highly toxic metals, the Oujé-Bougoumou we sampled were from about 3 to 12 times more likely (depending on the metal) to have indications that bodily uptake for environmental exposure was at a serious level.

Although objective scientific data on most behavioral or disease outcomes have been difficult to locate for the two Native American communities, a study of rates of asthma and wheezing among Kanesatake Mohawk children aged 0–18 recorded a prevalence of asthma (20.6 percent) almost twice that for Canadian children (11.2 percent) and triple that in the United States (6.91 percent). This finding deserves attention because heavy metal toxicity has been linked to asthma, and in the Kanesatake community, children often carry levels of toxins more than one standard deviation above the US median. Combined with informal reports of hyperactivity or other behaviors and diseases linked to toxins, evidence indicates that in this community and the Oujé-Bougoumou Cree, exposure and uptake of multiple toxins could often be linked to harmful effects.

The nine heavy metals are substantially higher in the 23 Oujé-Bougoumou than in comparable analyses of approximately 10000 normal males from the US. These elements include toxins that have been linked to health and behavioral dysfunction. Among them are mercury (which has multiple harmful effects and is present among the

Cree at exceptionally high levels) as well as lead, cadmium, manganese, and aluminum (chemicals which have been linked to learning disabilities, substance abuse, aggressive behavior, and disease). Because numerous elements are not present in excessively high levels among the Cree, these results do not seem to be an artifact of sampling or analytical processing.

The dangers of mercury toxicity, which have been widely discussed due to the effects of many dental amalgams, concern both "significant oxidative damage in the body" and interference with "the body's capacity to quench" other toxins. Among the 23 Cree sampled, mercury levels are 32 times those found in a baseline sample of 10000 Americans. The role of fish in the Oujé-Bougoumou diet and high levels of mercury in soil and water are likely to be responsible.

Because mercury has the effect of inhibiting the natural mechanisms of detoxification (such as glutathione), absorption of high levels of this toxin can make exposure to other toxic heavy metals even more dangerous than otherwise. To illustrate the magnitude of the effect, the ratio of the remaining eight heavy metals is abnormally high among the Oujé-Bougoumou compared to typical US residents. A ratio of 1.0 corresponds to levels of a toxin that would be similar among the Cree and Americans. Among the Oujé-Bougoumou Cree, levels of aluminum (often implicated in Alzheimer's disease) are over 5 times those in the American sample, and levels of lead (associated with hyperactivity, substance abuse, and violent crime) are 4 times those in the US. Although the functional effects of high levels of selenium and tin are not well understood, higher levels of manganese and cadmium have also been associated with higher rates of aggressive behavior and substance abuse.

Results of Study of the Kanesatake Mohawk

The environment of the Kanesatake Mohawk community, just west of the town of Oka, is impacted by toxins from an abandoned niobium mine. In addition to extensive mine tailings and contaminated water in open mine pits, the site was used for dumping drums of toxic waste. Although published data indicate levels above Canadian governmental guidelines for aluminum, iron, fluorides, manganese, and nitrites in liquid mine residues and for manganese and zinc in mine tailings, potentially dangerous levels of many other toxins are also reported and the location of these samples is not fully specified. There can be little doubt, however, that toxins are dispersed through a broad area. For example, in supporting the request of Niocan, a mining company, to reopen the mine in question, one recent legal document explicitly refers to contamination in agricultural lands near the abandoned mines.

To gain evidence of the potential for dangerous uptake of these toxins, head hair collected from an exploratory sample of 28 Kanesatake Mohawk was sent to Doctor's Data Laboratory. For over half (54 percent) of this sample, five or more elements were more than one standard deviation above the American median, and just under three-quarters (71 percent) had one or more elements over two standard deviations above the American median. This toxic burden was also indicated by the Total Toxic Exposure Index (TTEI), a measure used by Doctor's Data to indicate the overall threat posed by an individual's uptake of toxins. Using this measure, 63 percent of the Kanesatake sample had a toxic load above the 68th percentile (one standard deviation above the median for US samples), and 22 percent were above the 95th percentile (two standard deviations above the median).

Two toxins – manganese and antimony – are found in head hair more often than others. Manganese levels are more than one standard deviation above the US median in 16 of the 28 individuals tested, and above two standard deviations (over the 95th percentile) in 12 of them. High uptake of antimony exists at similar frequency: 14 individuals are above one standard deviation and 7 are above two. Other toxins are also often at dangerous high levels.

Measures of potency are important as well as measures of the frequency of dangerous levels of toxins. Of the metals tested in head hair, the Agency for Toxic Substances and Disease Registry (ATSDR) considers arsenic the highest priority based on both the relative toxicity per gram and the frequency of exposure at the national level. Although arsenic does not occur as frequently as manganese and antimony among those sampled, those with uptake of high levels of arsenic (over one standard deviation above the US median) are also likely to have been exposed to many other toxins. For example, among those with high levels of arsenic, five out of seven have similarly high levels of lead (considered second highest priority by ATSDR). Given the possibility of synergistic interactions among toxins, head hair is a useful biomarker of exposure because it provides data on multiple elements and compares uptake to national norms.

Identification of individuals who are particularly at risk makes it possible to recommend further examination and, if necessary, treatment. In the opportunistic sample of Kanesatake Mohawk, such cases are illustrated by six individuals (here identified only by initials) who are above the 95th percentile for Total Toxic Exposure Index.

1. TL (male, age 4) is above the 95th percentile for antimony, and above the 68th percentile for arsenic, lead, copper, silver, aluminum and gold.
2. SB (male, age 5) is above the 95th percentile for arsenic, antimony, and tin, and above the 68th percentile for lead, cadmium, chromium, selenium, silver, aluminum, uranium and gadolinium.
3. LB (female, age 33) is above the 95th percentile antimony and gadolinium, and above the 68th percentile for arsenic, lead, cadmium, cesium, manganese, palladium and tin.
4. DD (male, age 35) is above the 95th percentile for chromium, silver, antimony, aluminum and gadolinium, and above the 68th percentile for lead, zinc, manganese, palladium and titanium.
5. PB (male, age 41) is above the 95th percentile for arsenic, manganese and antimony, and above the 68th percentile for lead, aluminum, tin and gadolinium.
6. DN (male, age 49) is above the 95th percentile for antimony and tin, and above the 68th percentile for arsenic, chromium, manganese, aluminum, titanium and gadolinium.

Since two in this category are young boys, identification and treatment is clearly feasible for children.

Conclusions Based on Preliminary Studies

Levels of toxins found in the head hair of preliminary Cree and Mohawk samples are usually associated with exposures that pose serious dangers to health, normal cognition, and behavior. Dangers of lasting effects are particularly severe for very young infants, for whom toxins can disturb normal development of brain structures and hence have life-long effects While detailed epidemiological data for health and behavior are not available for either community, anecdotal evidence of high frequencies of behavioral and health dysfunctions and data on asthma among the Kanesatake Mohawk confirm the need and potential of further research among these populations.

CONCLUSION

For numerous types of social behavior, neuroscience points to revolutionary changes in our understanding of factors that influence humans, albeit often with different effects due to race, health, and income. With at least 80 million Americans taking Prozac or similar medications for depression, and perhaps as many as 11 million American children using Ritalin to control symptoms of hyperactivity (for example, ADHD), it should be no secret that brain chemistry influences human behavior. Nonetheless, social scientists have given little attention to evidence that dysfunctional behavior can be more likely when toxins like lead lower levels of essential neurotransmitters.

Conceptual changes in conventional social scientific research and public policies are needed when repeated studies show that dysfunctional behaviors can be associated with neurotoxins like lead, manganese, or silicofluoride. Consistent with their effects on neurotransmitters and behavior, the neurotoxins lead (Pb) and manganese (Mn) are often found in above-average levels among learning disabled children and violent criminals. Water treated with either hydrofluorosilicic acid (H2SiF6) or sodium silicofluoride (Na2SiF6) increases bodily absorption of these toxins and has other harmful effects on brain chemistry.

Public policies to reduce exposure to these toxins, whose sources are known, should therefore be given higher priority by American policy-makers. The geographic location of industrial releases of lead or manganese is recorded in the EPA'sToxic Release Inventory. Communities fluoridating water supplies with either fluorosilicic acid or sodium silicofluoride were recorded in the CDC's *Fluoridation Census 1992*, a 1007-page volume that's still useful but needs to be updated. More disturbing from both a practical and ethical perspective is evidence that the effects of these neurotoxins are substantially greater among Blacks than Whites.

Although knowledge of brain chemistry and behavior can identify sources of harm, the precise processes involved are complex and variable. For example, while the dangers of adding tetraethyl lead to gasoline were long known to some specialists, detailed evidence of its toxicity and harmful impact on health and behavior had not been widely documented even when this chemical was banned in 1991 (Kitman, 2000). Even today, the higher rates of violent crime, substance abuse, and learning deficits described below are not the target of effective public policies (Nevin, 2000; Masters, 2001).

To take a more striking case, even though the silicofluorides are highly corrosive and toxic metals, in 1950 their use was approved by the Public Health Service without testing on the "assumption" that the compounds H2SiF6 and Na2SiF6 "dissociate" into their component elements when added to water. Hence, 58 years after the introduction of water treatment with silicofluorides, all that was known of harmful effects from these compounds was "acute toxicity data." While not a direct test of silicofluoride treated water, this limited information would normally be a prudential reason not to embark on this policy without tests of safety under normal conditions of the proposed usage.

The assumption underlying the Public Health Service's original approval of silicofluoride use in 1950 was eventually confirmed over half a century later when dissociation of this compound was finally studied with appropriate laboratory experiments (Finney et al., 2006). Contrary to Westendorf's claim that incomplete dissociation was the basis of harmful effects from silicofluoride, Finney's laboratory experiments confirmed complete dissociation of silicofluorides. Contrary to the PHS conclusions from this fact, however, Finney's experiments also revealed the resulting biochemical effects included acetylcholinesterase inhibition. Because this enzyme controls the activity of acetylcholine, the main neurotransmitter in bodily movement, this confirmation of Westendorf's hypothesis is sufficient to explain the observed link between silicofluoride treated water and higher rates of impulsive behavior. This effect thus helps explain higher rates violent crime, of substance abuse, and learning deficits observed in communities where water supplies are treated with H2SiF6 or Na2SiF6.

To explore the scientific basis of such effects, the National Toxicology Program (NTP) of the National Institutes of Health had announced a project to study the new field of "toxicogenomics." This area of research expands the study of toxins to include the potential variability of reactions due to specific genetic mutations. The text of that announcement in the *Federal Register* (2002) provides a valuable introduction to this field:

> Toxicogenomics
> With the advent of novel molecular technologies, the NTP is moving into the arena of toxicogenomics, a new scientific field that examines how the entire genome is involved in biological responses of organisms exposed to environmental toxicants. Toxicogenomics studies the effect of toxicants on gene activity and specific proteins produced by genes in response to those toxicants.
>
> In an effort toward centralizing activities in toxicogenomics, the NIEHS/NIH established the National Center for Toxicogenomics (NCT) in September 2000. The NCT's mission is to coordinate a nationwide research effort for the development of a toxicogenomics knowledge base. Additional information about the NCT is available on the NIEHS website at: http://www.niehs.nih.gov/nct or by contacting the NTP Executive Secretary.

A specific question necessarily follows: will this new approach contribute to our understanding of human health and behavior in ways that improve public policy? Before providing illustrations of the importance of toxicogenomics for political decision-making, however, it is important to outline the changes in perspective needed to achieve these benefits. Toxicogenomics requires that we abandon the traditional dichotomy between "nature" and "nurture" as mutually exclusive explanatory categories, adopting instead approaches that integrate biological and social analyses of human behavior (Schubert et al., 1978; Abou-Donia et al., 2001a and 2001b; Masters et al., 1997).

The foregoing research indicates the need to include biochemical and environmental factors in the analysis, treatment, and prevention of behavioral dysfunctions and diseases that have long been analyzed in terms of the obsolete "nature – nurture" dichotomy. Conventional assessments of environmental pollution have focused on the presence of chemicals which have been identified as toxic. Such findings do not trace the uptake of these toxins and describe individual health or behavioral conditions associated with them. Completing the linkage between environmental releases and uptake influencing specific individuals is especially important because precise exposures and sensitivities vary.

The consequences are important for researchers in a number of the fields whose collaboration will often be needed. Criminologists who consider income, social class, education, and familial life have rarely imagined that brain chemistry and toxicology can help explain why some individuals are more sensitive that others to given environmental risk factors for criminal behavior. Toxicologists have often been content to sample one or two sites within a community, apparently unaware of the way differences between residences that are merely 100 meters apart can be associated with substantial differences in levels of extremely toxic metals. Physicians, psychiatrists, teachers, and parents treating ADHD are not aware that uptake of neurotoxins is often a crucial factor in hyperactivity and that, with chelation therapy, behavior can be greatly improved without the use of Ritalin or other medications.

For too long, "nature versus nurture" has been a theoretical dichotomy described in the abstract and defended with more heat than light. This dichotomy has meant that teaching and research in the biological sciences remains largely divorced from work in the social and policy sciences. In the age of human genetics, brain chemistry, and toxicogenomics, it is time to abandon this obsolete conceptualization of scientific knowledge. Whether describing the factors that might be producing high levels of ADHD in our school children or treating those who are afflicted, both political scientists and policy-makers need to consider scientific complexities unknown a generation ago. The same needs to be said of violent crime or substance abuse. Of course, it will take time to achieve such a profound transformation in entrenched ways of thinking. Hence the first steps in this direction should be a substantial expansion in undergraduate and graduate educational programs in such interdisciplinary fields as Human Biology, Cognitive Neuroscience, and Behavioral Genetics as well as Toxicogenomics.

BIBLIOGRAPHY

Abou-Donia, M.B., Goldstein, L.B., Jones, K.H., Abdel-Rahman, A.A., Damodaran, T.V., Dechkovskaia, A.M., Bullman, S.L. et al. (2001a), "Locomotor and Sensorimotor Performance Deficit in Rats following Exposure to Pyridostigmine Bromide, DEET, and Permethrin, Alone and in Combination", *Toxicological Sciences*, **60**, 305–14.

Abou-Donia, M.B., Goldstein, L.B., Dechkovskaia, A.M., Bullman, S.L., Jones, K.H., Herrick, E.A., Abdel-Rahman, A.A. et al. (2001b), "Effects of Daily Dermal Application of DEET and Permethrin, Alone and in Combination, on Sensorimotor Performance, Blood-Brain Barrier, and Blood-Testis Barrier in Rats", *Journal of Toxicology and Environmental Health*, Part A, **62**, 523–41.

Allard, André, Pelletier, Louis-Philippe and Savard, Michel (2000), *Healthy Homes, Healthy Families*, Saint-Jérôme, Quebec: Régie Régionale de la Santé et des Services Sociaux des Laurentides: Direction de la Santé Publique, pp. 24–5.

Angier, W. Kent (1993), "Behavioral Biomarkers to Identify Neurotoxic Effects", in Curtis Travis (ed.), *Use of Biomarkers in Assessing Health and Environmental Impacts of Chemical Pollutants*, New York: Plenum, pp.159–68.

Autissier, N., Rochette, L., Dumas, P., Beley, A., Loireau, A. and Bralet, J. (1982), "Dopamine and Norepinephrine Turnover in Various Regions of the Rat Brain after Chronic Manganese Chloride Administration", *Toxicology*, **24**(2), 175–82.

Boissonnault, Paul, Jean Demers, Daniel Labbé (2001), *Projet de Mine de Niocan, Inc. à Oka, Contre-expertise présentée à Conseil Mohawk de Kanesatake*, Dossier CPTAQ no. 318605 (Saint-Hyacinthe, Nov.).

Bratton, G.R., Hiney, J.K. and Dees, W.L. (1994), "Lead (Pb) Alters the Norepinephrine-induced Secretion of Leuteinizing Hormone Releasing Hormone from the Median Eminence of Adult Male Rats in vitro", *Life Sciences*, **55**(8), 563–71.

Bryson, Christopher (2004), *The Fluoride Deception*, New York: Seven Stories Press, pp. x–xi, 151–7, et passim.

Caspi, Avshalom, McClay, Joseph, Moffitt, Terrie E., Mill, Jonathan, Martin, Judy, Craig, Ian W., Taylor, Alan et al. (2002), "Role of Genotype in the Cycle of Violence in Maltreated Children", *Science*, **297**, 851–4.

Center for Disease Control (1992), *Fluoridation Census*, Washington, DC: U.S. Department of Health, Education, and Welfare.

Center for Disease Control (2001), CDC Press Release: "CDC releases new guidelines of fluoride use to prevent tooth decay", 16 August. Accessed at: http://www.cdc.gov/od/oc/media/pressrel/4r010817.htm.

Cohn, P.D. (1992), *An Epidemiological Report on Drinking Water and Fluoridation*, Trenton, NJ: New Jersey Department of Health.

Coplan, M.J. and Masters, R.D. (1999), "Is Silicofluoride Safe? Comments re EPA Response to Rep. Calvert's Inquiry", Submission to Representative Kenneth Calvert, Subcommittee on Energy and Science, Committee on Science, U.S. House of Representatives, 12 August.

Coplan, M.J. and Masters, R.D. (2001), "Guest Editorial: Silicofluorides and Fluoridation", *Fluoride: Quarterly Journal of the International Society for Fluoride Research*, **34**, 161–220.

Covel, C.L. (2001), "Sediment, Surface Water and Fish Quality Investigation: Oujé-Bougoumou Cree Nation Territory, Quebec, Canada", report submitted to The Grand Council of the Crees, 2 Lakeshore Road, Nemaska, Quebec, 4 September.

Croteau, Pierre-Yves (1991), *Etude de Risques Environnementaux et Physiques Associés à la Mine St-Lawrence Columbium: Rapport à Municipalité Paroisse d'Oka, QC*, Sodexen, Inc.

Federal Bureau of Investigation (2002), *Federal Crime Reports, Jan–Dec. 2001*, 24 June, Washington: FBI, accessed at: http://www.fbi.gov/ucr/01prelim.pdf.

Federal Register (2002), August 19, 2002 (Vol. 67, No. 160], pp5380–10.

Finney, W.F., Wilson, E., Callender, A., Morris, M.D. and Beck, L.W. (2006), "Reexamination of Hexafluorosilicate Hydrolysis by ^{19}F NMR and pH Measurement", *Environmental Science & Technology*, **40**, 2572–7.

Fox, J.C. (1999), "Letter from EPA Assistant Administrator," May 10. Cf. M.J. Coplan and Roger Masters, "Is Silicofluoride Safe?", Comments re EPA Response to Rep. Calvert's Inquiry," submission to Representative Kenneth Calvert, Subcommittee on Energy and Science, Committee on Science, U.S. House of Representatives (August 12, 1999).

Franklin, Benjamin (1786 [1987]), "Letter to Benjamin Vaughan 'On the bad Effects of Lead taken inwardly'", 31 July 1786, in J.A.L. Lemay (ed.), *Complete Writings of Benjamin Franklin*, New York: Library of America, pp.1163–6.

Gottschalk, L., Rebello, T., Buchsbaum, M.S., Tucker, H.G. and Hodges, H.L. (1991), "Abnormalities in Trace Elements as Indicators of Aberrant Behavior", *Comprehensive Psychiatry*, **342**, 229–37.

Hara, T., Miyazawa, K. and M. Miyamoto, M. (2002), "Properties of Copper Interconnection Layers Deposited by Electroplating Using a Copper Hexafluorosilicate Electrolytic Solution", *Electrochemical and Solid-State Letters*, **5**, C1-3.

Kirpekar, S.M., Dixon, W. and Prat, J.C. (1970), "Inhibitory Effect of Manganese on Norepinephrine Release from the Splenic Nerves of Cats", *Journal of Pharmacology and Experimental Therapeutics*, **174** (1), 72–6.

Kitman, Jamie Lee (2000), "The Secret History of Lead", *The Nation*, **270**, March.

Knappwost, A. and Westendorf, J. (1974), "On the Inhibition of Acetylcholinesterase by Fluoride", *Naturwissenschaft*, **61**, 274–5.

Maas, Richard P., Patch, Steven C., Christian, Anna-Marie and Coplan, Myron J. (2007), "Effects of Fluoridation and Disinfection Agent Combinations on Lead Leaching from Leaded-brass Parts", *NeuroToxicology*, **28**, 1023–31.

Massie, Tara L. (2010), *Manganese Exposure Alters Extracellular Norepinephrine, Norepinephrine Receptor and Transporter Protein and mRNA Levels in the Developing Rat Brain*, Ph.D. thesis, Winston Salem, NC: Wake Forest University.

Masters, R.D. (2001), "Silicofluorides and Higher Blood Lead: A National Problem that Particularly Harms Blacks", 15 November, Video conference, Appalachian Environmental Lab, Frostburg, MD.
Masters, R.D. (2002), "Neurotoxicology and Violence", in Richard W. Bloom and Nancy K. Dess (eds), *Evolutionary Psychology and Violence: A Primer for Policymakers and Public Policy Advocates*, Westport, CN: Praeger.
Masters, R.D. and Coplan, M. (1999a), "A Dynamic, Multifactorial Model of Alcohol, Drug Abuse, and Crime: Linking Neuroscience and Behavior to Toxicology", *Social Science Information*, London: Sage, pp. 591–624.
Masters, R.D. and Coplan, M. (1999b), "Water Treatment with Silicofluorides and Lead Toxicity", *International Journal of Environmental Studies*, **56**, 435–49.
Masters, R.D. and Coplan, M.J. (forthcoming), "The Triune Brain, the Environment, and Human Behavior: Homage to Paul MacLean", in Russell Gardner (ed.), *Festschrift in Honor of Paul MacLean.* First presented at Back Bay Hilton Hotel, Boston, MA, 16 July 1999.
Masters, R.D., Coplan, M.J., Hone, B.T. and Dykes, J.E. (2000), "Association of Silicofluoride Treated Water with Elevated Blood Lead", *Neurotoxicology*, **21**, 1091–100.
Masters, R.D., Hone, B. and Doshi, A. (1998), "Environmental Pollution, Neurotoxicity and Violent Crime", in J. Rose (ed.), *Aspects of Environmental Toxicology*, London: Gordon and Breach, pp13–48.
Masters, R.D., with Brian T. Hone, David J. Grelotti, David Gonzales and David Jones (1997), "Environmental Pollution and Crime", *Vermont Law Review*, **22** (Winter), 358–82.
Masters, R.D., with Baldwin Way, Brian T. Hone, David J. Grelotti, David Gonzalez, and David Jones (1998), "Neurotoxicity and Violence", *Vermont Law Review*, **22**, 358–82.
Masters, R.D. and Coplan, M., with Brian T. Hone, David J. Grelotti, David Gonzales and David Jones (1999), "Brain Biochemistry and the Violence Epidemic: Toward a 'Win–Win' Strategy", in Stuart Nagel (ed.), *Super-Optimizing Examples: Across Public Policy Problems*, Hauppauge, NY: Nova Science Publishers.
National Research Council (1997), *Safe Water from Every Tap* Washington, DC: National Academies Press.
Needleman, Herbert (ed.) (1989), *Human Lead Exposure*, Boca Raton, FL: CRC Press.
Nevin, Rick (2000), "How Lead Exposure Relates to Temporal Changes in IQ, Violent Crime, and Unwed Pregnancy", *Environmental Research, Section A*, **83**, 1–22.
OECD (2008), "OECD in Figures", *OECD Observer 2008*, Paris: OECD, pp.8–9.
OECD (2009), "OECD in Figures", *OECD Observer 2009*, Paris: OECD.
Office of Research and Development, EPA (2002), "Biomarkers for the Assessment of Exposure and Toxicity in Children", Science to Achieve Results (STAR) Program, Washington, DC: National Center for Environmental Research, US Environmental Protection Agency, p11, available at: http://es.epa.gov/ncer/rfa/02biomarchild.html.
Quig, David W. (1997), "Heavy Metals and the Difficult to Diagnose Patient", *The Internist* September, pp. 11–13.
Reeves, T.G. (1994), *Water Fluoridation: A Manual for Engineers and Technicians* (U. S. Public Health Service, CDC Division of ORAL HEALTH, APRIL 1994).
Reif, John S., Ramsdell, Howard S., DuTeau, Nancy M., Anger, W. Kent and Tsongas, Theodora A. (1993), "The Use of Biomarkers in the Evaluation of Exposure and Health at a Hazardous Waste Site", in Curtis Travis (ed.), *Use of Biomarkers in Assessing Health and Environmental Impacts of Chemical Pollutants*, New York: Springer Science + Business Media, pp227–35.
Rymer, Andrew (2000), *The (Political) Science of Fluoridating Public Water Supplies*, Senior Honors Thesis, Dartmouth College, Hanover, NH.
Schubert, Jack, Riley, E. Joan and Tyler, Sylvanus A. (1978), "Combined Effects in Toxicology – a Rapid Systematic Testing Procedure: Cadmium, Mercury, and Lead", *Journal of Toxicology and Environmental Health*, **4**, 763–76.
Seavey, J. (2005), "Water Fluoridation and Violent Crime in America", *Fluoride*, **38**, 11–22.
Shabecoff, Philip and Shabecoff, Alice (2008), *Poisoned Profits: The Toxic Assault on Children*, New York: Random House.
Struempler, Richard E., Larson, Gerald E. and Rimland, Bernard (1985), "Hair Mineral Analysis and Disruptive Behavior in Clinically Normal Young Men", *Journal of Learning Disabilities*, **18**, December, 609–12.
Struzynska, L. and Rafalowska U. (1994), "The Effect of Lead on Dopamine, GABA and Histadine Spontaneous and KCL-dependent Releases from Rat Brain Synaptosomes", *Acta Neurobiologiae Experimentalis (Wars)*, **54**(3), 201–207.
Thomassin, Yves et al. (2001), "Observations Écrites de Niocan, Inc. Suite à l'Avis de Changement du 2 avril 2001; Dossier CPTAQ no. 318605, 21 May, Sainte Foy, Québec: Roche.
Turnau, Robert B. (2000), Letter to Roger D. Masters from Chief, Treatment Technology Evaluation Branch, Water Supply and Water Resources Division, Cincinnati: National Risk Management Research Laboratory, USEPA, 16 November.

Waldbott, G.L., Burgstahler, A.W. and McKinney, H.L. (1978), *Fluoridation: The Great Dilemma*, Lawrence, KS: Coronado Press.

Westendorf, Johannes (1975), "Die Kinetik der Acetylcholinesterase Hemmung und Die Jonen", Doctoral Dissertation, Universitat Hamburg Fachbereich Chemie, Hamburg.

Wilson, Jim (1999), "The Chemistry of Violence", *Popular Mechanics*, April, pp.42–3.

Wright, J.P., Dietrich, K.N., Ris, M.D., Hornung, R.W., Wessel, S.D., Lamphear, B.P., Ho, M. et al. (2008), "Association of Prenatal and Childhood Blood Lead Concentrations with Criminal Arrests in Early Adulthood", *PLoS Med*, **5**(5), e101.

Zuch, C., O'Mara, D.J., Corey-Slechta, D.A. (1998), "Low-level Lead Exposure Selectively Enhances Dopamine Overflow in Nucleus Accumbens: An In Vivo Electrochemistry Time Course Assessment", *Toxicology and Applied Pharmacology*, **150**(1), 174–85.